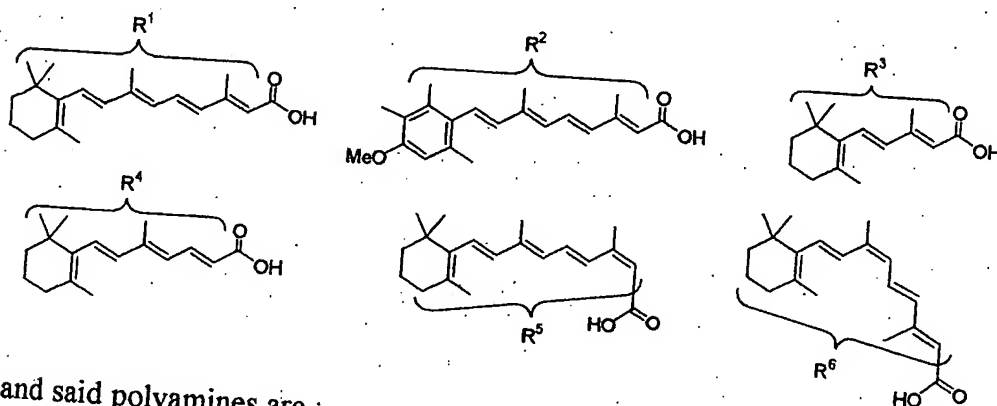


It is to be understood that, while the foregoing invention has been described in detail by way of illustration and example, numerous modifications, substitutions and alterations are possible without departing from the spirit and scope of the invention as described in the following claims.

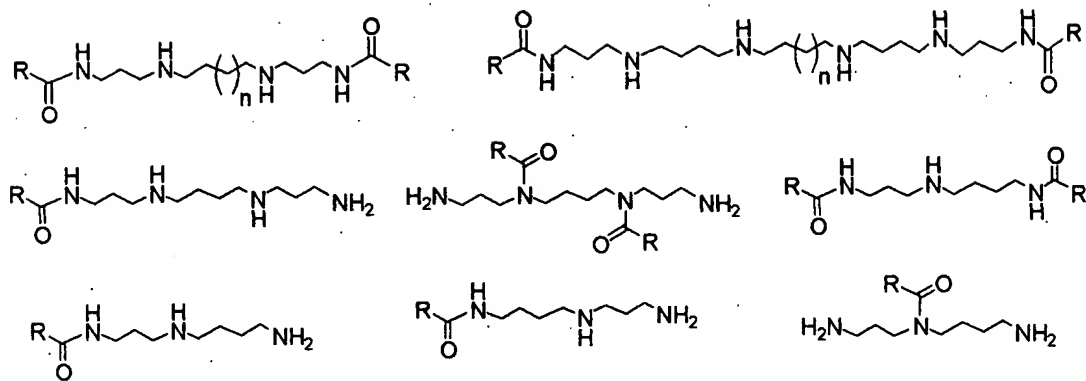
What is claimed is:

1. Conjugates of polyamines with acidic retinoids and in particular polyamine amides in which the R group of the acyl group(s) RCO is one of the retinoid residues R<sup>1</sup>-R<sup>6</sup> pointed out in the following pharmaceutically important acidic retinoids and polyene chain-shortened *all-trans*-retinoic acid analogues:



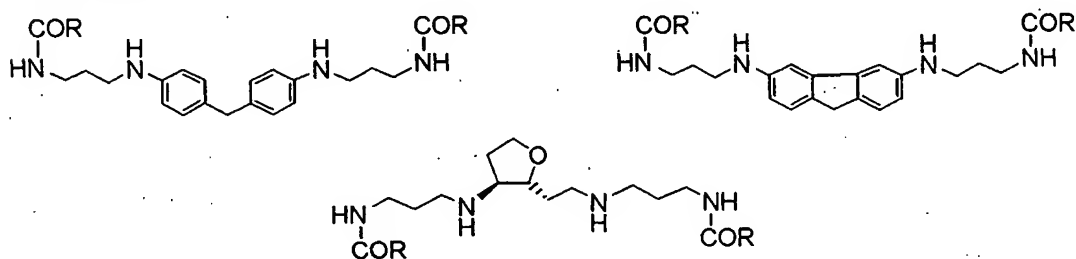
and said polyamines are:

- a) Linear tri- and tetra-amines, which conjugates have the following general formulae:

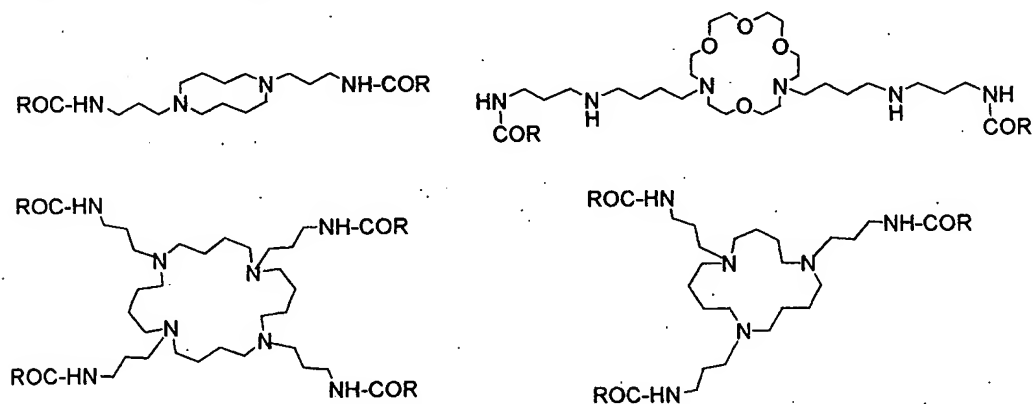


wherein  $n$  is 1 to 9

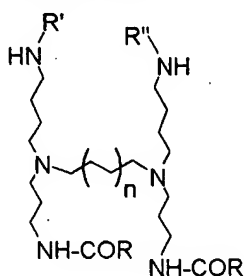
b) conformationally restricted, which conjugates have the following general formulae:



c) cyclic, which conjugates have the following general formulae :



d) branched (dimeric), which conjugates have the following general formula :

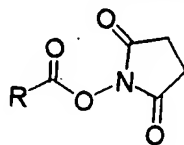


wherein

$R'$  is COR or  $(CH_2)_3NHCOR$  and  $R''$  is COR or  $(CH_2)_3NHCOR$

2. A method for the preparation of a compound according to claim 1 characterized in that it involves either the following two steps:

a) synthesis of compounds with the general formula



wherein R is one of the retinoid residues  $R^1$ - $R^6$  of claim 1, which involves esterification of acidic retinoids with HOSu in the presence of the coupling agent DCC and purification with flash column chromatography

b) direct selective acylation of the primary amino groups of polyamines with the as above obtained compounds,  
or the acylation of the secondary amino groups of polyamines, protected at their primary amino functions with the trifluoroacetyl or the 9-fluorenylmethoxycarbonyl group, with the acidic retinoids of claim 1 in the presence of the coupling agent PyBrOP, followed by deprotection.

3. A method according to claim 2 characterized in that it involves the direct selective acylation of the primary amino functions of polyamines or their corresponding hydrochloride or trifluoroacetate salts with the compounds of step a) of claim 2, wherein the solvent is selected between dichloromethane, chloroform and dimethylformamide and the base, where necessary, is selected between triethylamine and diisopropylethylamine or any other tertiary amine or in general any other non-nucleophilic base.
4. A method according to claim 3 characterized in that the selective acylation of the primary amino functions of polyamines is effected with any other activated carboxylic acid derivative known to acylate selectively primary amino functions in the presence of secondary ones.

5. A method according to claim 2 characterized in that the selective mono- or bis-acylation of primary amino functions of polyamines takes place indirectly and involves the following steps :

- (i) protection of the secondary amino functions of polyamines, bearing the trityl protecting group at their primary amino functions, with the 9-fluorenylmethoxycarbonyl or the trifluoroacetyl group
- (ii) detritylation
- (iii) mono- or bis-acylation with the compounds of step a) of claim 2
- (iv) complete deprotection and purification, if necessary, by flash column chromatography.

6. A method according to claim 2 characterized in that the selective acylation of the secondary amino functions of polyamines involves the following steps:

- (i) selective trifluoroacetylation of the primary amino functions of polyamines
- (ii) acylation of the secondary amino functions with the acidic retinoids of claim 1 in the presence of the coupling agent PyBrOP
- (iii) removal of the trifluoroacetyl groups by alkaline hydrolysis.

7. Pharmaceutical preparations or products containing the compounds claimed in claim 1 for therapeutical applications in humans